Tailoring carbon nanotubes surface chemistry for the purification of antileukemic drugs

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Abstract
Biopharmaceuticals have been used to overcome fatal diseases related with aging. L-aspariginase (LA), in particular, has shown evidences of being efficient for leukemia therapy. The LA production and purification require several steps increasing the cost of the process. In this work, functionalized carbon nanotubes (CNTs) were studied as a cost-effective support to purify LA. It was shown that CNTs have strong affinity for the target biopharmaceutical, meaning that can be a promising alternative for the adsorption and purification of LA.

Author Keywords. Carbon nanotubes, antileukemic drugs, L-asparaginase, purification

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1. Introduction

Nowadays, the average life expectancy is steadily increasing. However, there are still several fatal diseases normally associated with aging, such as cancer, heart and neurological diseases. Biopharmaceuticals as nucleic-acid-based products, antibodies and recombinant proteins and enzymes are applied to overcome these age-related diseases. L-aspariginase (LA) is one of the most widely used therapeutic enzymes and has been proven efficient for the treatment of acute and chronic lymphoblastic leukemia, Hodgkin's disease and different types of melanomas (Uygun 2017).

The main problem associated with the therapeutic use of LA is the difficulty in its production and purification. LA is produced *via* fermentation and its purification is usually comprised by several steps, which can include precipitation, liquid-liquid extraction and chromatography techniques (Tundisi et al. 2017). High yield and purity require long processing times and a consequent increase of process costs. Therefore, the development of a cost-effective production/purification process is of emerging concern.

In the present work, reusable functionalized nanomaterials, namely CNTs, were studied to obtain sustainable and low-cost purification techniques for the target enzyme. The surface of CNTs was chemically modified by different treatments to understand the behavior of the enzyme in contact with the nanomaterial.

2. Materials and Methods

Commercial multi-walled carbon nanotubes, purchased from NANOCYL^{TM} (NC3100), were subjected to different hydrothermal treatments by oxidation of the pristine CNTs: i) with 10

M nitric acid (HNO_3) at boiling temperature; and ii) with 0.05, 0.1, 0.2 and 0.3 M HNO_3 in an autoclave. The obtained materials were characterized by N_2 adsorption isotherms at 77 K, temperature programmed desorption, thermogravimetry, infrared and ultraviolet–visible spectroscopy, X-ray diffraction and electron microscopy. Commercial LA was used for preliminary tests. Experimental conditions, such as pH, material/LA mass ratio and contact time were optimized. LA activity was assessed by Nessler reaction, which quantifies the amount of ammonium released after the enzymatic reaction (Magri 2018).

3. Discussion

Results revealed that depending on the CNTs surface chemistry, different values of recovered LA activity were achieved. The pH and material/LA ratio also influence the adsorption of LA on the material surface. CNTs treated with 0.3 M HNO_3 in an autoclave were more efficient to adsorb LA, which may be attributed to the larger content on oxygen surface groups. Although total adsorption of LA by CNTs was obtained, the experimental conditions will be fully optimized for maximizing the recovered activity by LA.

4. Conclusions

CNTs were successfully functionalized with oxygen-containing surface groups by different thermal routes. LA was easily attached to CNTs by simple adsorption. CNTs supports can be considered as a promising alternative to pre-established high-cost methods for the adsorption and purification of LA.

References

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